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Slofstra, Christien; Klein, Nicola S.; Nauta, Maaïke H.; Wichers, Marieke; Batalas, Nikolaos; Bockting, Claudi L.H.

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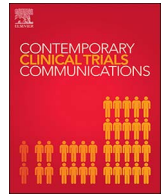
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Imagine your mood: Study design and protocol of a randomized controlled micro-trial using app-based experience sampling methodology to explore processes of change during relapse prevention interventions for recurrent depression

Christien Slofstra^a, Nicola S. Klein^a, Maaïke H. Nauta^a, Marieke Wichers^b, Nikolaos Batalas^c,
Claudi L.H. Bockting^{a,d,*}

^a Department of Clinical Psychology and Experimental Psychopathology, University of Groningen, 9712 TS, Groningen, The Netherlands

^b University of Groningen, University Medical Center Groningen (UMCG), Department of Psychiatry (UCP), Interdisciplinary Center for Psychopathology and Emotion Regulation (ICPE), 9700 RB, Groningen, The Netherlands

^c Department of Industrial Design, Eindhoven University of Technology, 5612 AZ, Eindhoven, The Netherlands

^d Department of Clinical Psychology, Utrecht University, 3508 TC, Utrecht, The Netherlands

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ABSTRACT

Background: Relapse prevention strategies include continuation of antidepressant medication and preventive psychological interventions. This study aims to gain understanding that may inform tailoring of relapse prevention to individual differences, to improve their effects. Such treatment personalization may be based on repeated assessments within one individual, using experience sampling methodology. As a first step towards informing decisions based on this methodology, insight is needed in individual differences in risk of relapse and response to treatment, and how relapse prevention strategies may differentially target vulnerability for relapse. **Methods:** The smartphone application ‘Imagine your mood’ has been developed specifically for this study to assess emotions, imagery, cognitions, and behaviors in daily life. Parallel to the randomized controlled trial ‘Disrupting the rhythm of depression’, 45 remitted recurrently depressed individuals taking continuation antidepressant medication will be randomly assigned to either continuing antidepressant medication ($n = 15$), continuing antidepressant medication combined with an eight-session preventive cognitive therapy ($n = 15$), or tapering of antidepressant medication in combination with preventive cognitive therapy ($n = 15$). Relapse and return of depressive symptomatology over a 24-month follow-up will be assessed. Additionally, matched never depressed individuals ($n = 15$) will be recruited as controls.

Discussion: This innovative study combines the strengths of a randomized controlled trial and experience sampling methodology in a micro-trial to explore individual differences in risk of relapse and what works for whom to prevent relapse. Results may ultimately pave the way for therapists to tailor relapse prevention strategies to individual (affective) vulnerability.

Trial registration: ISRCTN15472145, retrospectively registered.

1. Introduction

Major Depressive Disorder (MDD) poses a heavy burden on patients and society [1–3]. The highly recurrent nature of MDD [4,5] adds greatly to the burden of depression [6,7]. With every previous episode the risk of relapse increases, so that after having experienced two or more depressive episodes the chance of relapse is 60–90% [8–10]. Reducing the burden of MDD therefore crucially involves prevention of recurrence in previously depressed individuals.

Although both continuation of antidepressant medication (ADM) [11,12] and psychological interventions [13–17] can reduce the risk of relapse, many previously depressed individuals do relapse in the long run. Individual patients may differ in their vulnerability for relapse. Identifying these individual differences and understanding how different relapse prevention strategies target these vulnerabilities may enable therapists to further tailor interventions [18]. Crucial questions therefore seem to be what works best for whom [19,20]. However, empirical evidence guiding such personalized relapse prevention

* Corresponding author. Department of Clinical & Health Psychology, Utrecht University, 3508 TC, Utrecht, The Netherlands.
E-mail address: c.l.h.boeking@uu.nl (C.L.H. Bockting).

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strategies is scarce [21]. To date, attempts to identify single individual characteristics that determine treatment response have not resulted in consistent moderators of effect that may inform treatment decisions [18,22].

Experience sampling method (ESM) [23–25] offers a route towards personalized interventions [26]. By repeatedly assessing emotions, cognitions, and behaviors in the flow of daily life, ESM allows for assessment of their interrelations, temporal dynamics and change over time. Furthermore, integrating ESM in clinical practice may empower patients [27] and provide feedback to both patients and therapists, with positive long-term results [28]. Further advantages of ESM are minimization of retrospective biases, which may be particularly relevant in depression [29], and maximized ecological validity by random sampling in daily life [24]. ESM may be ideally suited for informing and optimizing personalized treatments [30]. However, for applying ESM to the individual patient, insight is needed in individual differences in vulnerability for relapse and early response to treatment. Also, understanding of the working mechanisms of different relapse prevention strategies is needed.

This report aims to describe the theoretical rationale and study design for ‘Imagine your mood’, an innovative study exploring the potential for using ESM for informing personalized relapse prevention. In the ‘Imagine your mood’ study, data of both previously depressed and matched never depressed individuals will be collected. ESM will be added to a three-arm relapse prevention trial ‘Disrupting the rhythm of depression’ [31]. This randomized controlled trial (RCT) investigates PCT while either continuing or tapering ADM as a relapse prevention strategy compared to continuation ADM in a sample of individuals diagnosed with remitted recurrent MDD.

2. Method

2.1. Theoretical rationale

2.1.1. Relapse prevention strategies

Relapse prevention often consists of continuation of antidepressant medication (ADM) after the acute phase of depression [32]. Meta-analyses show that ADM reduces risk of relapse [11,12]. However, many ADM users experience adverse side effects such as weight gain, sexual problems, and emotional numbing [33,34]. In addition, many ADM users have difficulty with long-term adherence to ADM [35,36]. Discontinuation of ADM may also be problematic as individuals who wish to discontinue or taper their ADM may be hampered by withdrawal symptoms [37] and discontinuing their ADM may leave them more vulnerable to relapse [14,38,39].

Most patients prefer psychological treatment strategies [40,41]. Several psychological interventions have been developed specifically for preventing relapse in depression, i.e. preventive cognitive therapy (PCT) [42], mindfulness-based cognitive therapy (MBCT) [43], and wellbeing cognitive therapy [44]. Meta-analyses conclude that preventive psychological therapies reduce risk of relapse [13–17], possibly even more than continuation of ADM after the acute phase of depression does [17]. Recently, two randomized controlled trials (RCTs) have examined whether one of these psychological interventions (MBCT) may be a viable alternative to continuation of ADM for preventing relapse in depression. These studies show mixed results. Kuyken et al. [45] found no difference in relapse rates within 24 months for a group of remitted recurrently depressed participants that continued ADM (49%, $n = 212$) compared to a group that received MBCT with ADM tapering (44%, $n = 212$). Huijbers et al. [46], however, found significantly higher relapse rates (over 15 months) for the group that received MBCT and tapered ADM (54%, $n = 128$) versus the group that received MBCT and continued ADM (39%, $n = 121$).

Thus, although both continuation of ADM [11,12] and psychological interventions [13–17] can reduce the risk of relapse, many previously depressed individuals do relapse in the long run.

2.1.2. Experience sampling methodology

ESM data can be used to model temporal dynamics and individual networks in accordance with a network perspective on depression. In this perspective, depression is conceptualized as a complex dynamical system of interacting symptoms, cognitions, emotions, and behaviors. Relapse may then be conceptualized as a transition of the network into a depressive state [47]. Given that depression is highly heterogeneous [48], these networks may vary greatly between individuals and ESM may be used to construct personalized networks. These individual networks potentially contain indicators of vulnerability for relapse, including early warning signals of relapse within an individual [49].

A body of empirical literature is rapidly emerging that supports the potential for ESM to contribute to personalizing interventions in depression [30]. First, preliminary studies support the hypothesis that ESM provides information on vulnerability for relapse. Recently, temporal dynamics of affect have been hypothesized to signal sudden transitions into and out of a depressive state. Indeed, higher inertia (the degree to which current states can be predicted from previous states) was found in individuals at the brink of relapse [49]. Higher inertia of negative affective in particular is hypothesized to signal relapse [49]. Crucially, increased inertia within an individual may be an early warning signal of relapse. First evidence of such increased inertia was demonstrated in a previously depressed individual that attempted to taper his ADM [50]. The generalizability of this single case study is limited and requires replication. However, these findings demonstrate that individual networks may contain information about vulnerability for relapse. Further insight is needed in individual differences in these vulnerabilities.

Second, ESM allows for in-depth analyses of interrelations between cognitive mechanisms and affective vulnerabilities for relapse. For example, an ESM design was used previously to examine the hypothesis that the negative affective impact of rumination contributes to depressive symptomatology [51]. Another mechanism of interest is mental imagery, frequently described as “seeing with the mind’s eye” [52]. Mental imagery has been related to stronger emotional responses to positive and negative stimuli [53,54]. However, it is unclear how mental imagery influences affect dynamics in daily life. Thus, ESM may elucidate mechanisms that underlie vulnerability for relapse within a group of previously depressed individuals.

Third, ESM may be used to monitor early responses during different treatment strategies that may predict whether an individual will benefit from a treatment. The previously mentioned single case study [50] suggests that ESM may be used to monitor such early responses in individuals using different relapse prevention strategies. In acute depression, early changes in affect were found predictive of treatment outcome [55]. Affective disturbances may play a central role in the depressive network [56], given that depression is an emotional disorder [57]. The importance of affect after remission as a risk factor for depressive relapse is supported by the finding that mood as assessed using a one-item visual analogue scale (VAS) running from happy to sad has been found predictive of relapse [58] even after five and a half years [59]. ESM may capitalize on this predictive value of affect, by examining whether early affective changes indicate whether an individual will for example be able to successfully taper ADM. However, whether early affective changes predict treatment outcome of different relapse prevention strategies has not yet been examined.

Fourth, ESM may provide new insights on potential mechanisms by which treatment strategies prevent depressive relapse. Psychological interventions and ADM may target vulnerability for relapse in different manners. This was first illustrated with ESM data in a study that investigated the effect of MBCT for individuals with residual depressive symptomatology. Using ADM during MBCT facilitated decrease in negative affect, but hampered increase in positive affect [60]. However, causal inferences based on this study are limited because the use of ADM was not randomly assigned. This study demonstrates that ESM may be used for uncovering differential pathways by which relapse

prevention strategies may target affect in daily life. These differential effects of relapse prevention strategies may ultimately be used for tailoring interventions to individual affective vulnerability.

In sum, there are at least four routes to furthering personalized relapse prevention using ESM: exploring individual differences in vulnerability for relapse, examining (cognitive) mechanisms that contribute to (affective) vulnerability, interpreting early changes in response to treatment, and examining what mechanisms are differentially targeted by relapse prevention strategies.

2.1.3. Aims and hypotheses

The first aim of the ‘Imagine your mood’ study is to explore individual differences in vulnerability for future relapse. In addition to exploring between-individual differences, within-individual affective change will be explored as a potential precursor for relapse. It is hypothesized that within-individual increases in negative affect and negative affective inertia may precede relapse. It will be examined whether such individual affective trajectories are specific to individuals at high risk of depressive relapse by examining these in a never depressed control group as well. Second, how cognitive mechanisms interact with affective vulnerability for relapse will be examined. Specifically, how mental imagery is related to affect in daily life will be investigated. Third, it will be examined whether early affective changes may be associated with successful tapering of ADM. It is hypothesized that affective improvements in the first two weeks of tapering may be associated with successful tapering of ADM. Fourth, it will be explored how relapse prevention strategies may differentially target vulnerability for relapse by group-based comparison of the networks in the three arms of the RCT. Finally, several secondary outcome measures will be included for hypothesis-generating purposes. In sum, this study combines the strengths of an RCT and ESM in a micro-trial to explore processing of change during different relapse prevention strategies.

3. Study design

This study is designed as a micro-trial that includes ESM to explore processing of change during different relapse prevention strategies. Participants ($N = 45$) will be randomly allocated to either continuing ADM ($n = 15$), continuing ADM combined with an eight-session PCT ($n = 15$), or tapering of ADM in combination with PCT ($n = 15$). Current and previous depressive episodes will be monitored using telephonic interviews at the start of the study and after three, nine, 15, and 24 months. The ESM procedure will take place during the first eight weeks of the study (parallel to the PCT training for those individuals randomly allocated to receive PCT). Data of a never depressed control group will be collected.

The addition of ESM to the RCT ‘Disrupting the rhythm of depression’ (Netherlands Trial Register: [NTR1907](#)) was approved by the medical ethical board of the University Medical Center Groningen (METc 2009/158). Ethical approval for including never depressed individuals has been obtained from the University of Groningen Ethical Committee of the Psychology Department (ppo-014-043). This study is funded by ZonMW: The Netherlands Association for Health Research and Development (171002401 and OOG Grant 100002035) and by NWO, the Netherlands Organization for Scientific Research (022.003.038).

3.1. Sample

The previously depressed sample will be recruited parallel to the three-armed RCT ‘Disrupting the rhythm of depression’ [31]. To be included, participants have to be diagnosed with remitted, recurrent MDD, as defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV) and assessed by trained interviewers using the Structured Clinical Interview for DSM–IV disorders (SCID-I) [61]. Further inclusion criteria are a current score of ≤ 10 on the Hamilton

Rating Scale for Depression (HRSD) [62], and use of continuation ADM in the last six months. Exclusion criteria are current mania or hypomania or a history of bipolar illness, any psychotic disorder (current and previous), organic brain damage, alcohol or drug dependency/abuse, and predominant anxiety disorder. After inclusion, participants will be randomly allocated to one of the three arms of the study.

The matched never depressed sample will be recruited via advertisements on social media, posters, and word of mouth. Participants will be selected to match the previously depressed sample on age, gender, and educational level. Exclusion criteria are current or previous depressive episodes as assessed with the SCID-I, and use of ADM. Participants will receive a 10 euro gift certificate.

3.2. Procedure

The procedure as described in the trial protocol of the RCT [31] will be followed, with the adjustments that PCT will be administered individually rather than in groups, and the addition of the ESM procedure. Participants randomized to a PCT condition will receive eight weekly sessions of individual PCT, administered by trained psychologists using the treatment manual [63]. Participants randomized to ADM continuation (with or without PCT) will be advised to continue ADM in line with leading clinical guidelines [32,64] and their general practitioner or psychiatrist will also be informed. For participants randomized to the tapering condition, the instruction will be to gradually taper ADM in four weeks guided by their general practitioner or psychiatrist, who will also be informed and advised.

3.3. Experience sampling method

The experience sampling app ‘Imagine your mood’ has been developed and programmed using TEMPEST software [65]. This app will enable participants to fill out the questionnaires on their own smartphone. If needed, a research-smartphone will be made available to participants. The questionnaire includes a section on affect and emotions, followed by questions about cognitions and imagery, and finally a section on activities. The application has been programmed to set triggers for questionnaires ten times a day, three days a week (on Thursdays, Fridays, and Saturdays), for eight weeks, resulting in a maximum of 240 responses. The triggers are set semi-randomly, with one trigger per 90-minute interval between the hours of 7.30 and 22.30, and a minimum of 30 min between triggers.

During an approximately one-hour face-to-face briefing, a trained assistant will install the app on the smartphone of a participant, explain the ESM procedure, elucidate the more difficult concepts, help practice the questionnaire, and answer any questions. Participants will be instructed to respond to a trigger as soon as possible, and answer the questionnaire about the moment just before the trigger. Participants will not be informed about the five-minute time limit that is set on the questionnaire; they will be instructed that they are too late if the questionnaire is no longer available. Participants will receive weekly brief structured telephonic interviews to monitor the functionality and use of the ‘Imagine your mood’ app. Participants will be invited to contact their assistant for questions or technical difficulties. An overview of assessments is provided in [Table 1](#).

3.4. Measures

To examine the research questions, the following measures will be used.

3.4.1. Affect

Momentary mood will be assessed with the mood scale [59]. Participants rated the question “at the moment, I feel ...” on a VAS ranging from happy (0) to sad (100).

Adjectives to assess positive affect and negative affect were selected

Table 1
Overview of assessments.

Instrument	Baseline	ESM study period	Follow-up period (in months)			
			3	9	15	24
SCID-I	+		*	*	*	*
HRSD	+		*	*	*	*
ESM		+ (8 weeks)				
Weekly calls		+ (8 weeks)				

Note. SCID-I = Structured Clinical Interview for DSM-IV disorders, HRSD = Hamilton Rating Scale for Depression, ESM = Experience sampling methodology, + Both previously depressed and never depressed individuals, * Previously depressed individuals only.

based on previous research [66] and the adjectives described in the diagnostic criteria of a depressive episode [57], and discussions in our research team. Ratings of the adjectives (on a 0–100 VAS) will be averaged to a positive affect (*cheerful, enthusiastic, hopeful, content, energetic*) and a negative affect (*anxious, angry, lonely, irritated, down, suspicious, helpless, guilty, insecure*) scale per moment per individual.

3.4.2. Degree of mental imagery

First, participants will be presented with instructions to identify what they had in mind just before the trigger, i.e. their mental representation. In the briefing, participants will be familiarized with this procedure and instructed as follows “*you (almost) always have something in mind. Please take your time to recall what you had in mind just before the trigger. If you do not remember what you had in mind just before the trigger, please select the most recent thing you had in mind that you can remember.*”

Participants will receive the following information about mental imagery: “*Sometimes you see things in mind, while you do not see those with your eyes at that moment. For example, when you recall a memory or when you imagine yourself doing something in the future. You can also experience this with other sensory modalities. With hearing, for example, when you have a song in your head. Can you for example remember the last time you did groceries, or that you were on vacation? What do you see in your mind's eye? Can you hear the sounds in the memory? Or feel a physical sensation, like the sun on your face or perhaps an itch?*”

Participants will rate the degree of visual mental imagery answering the question “I see it in my mind's eye” on a VAS running from 0 to 100. Non-visual mental imagery will be assessed with the questions “(it) is an auditory sensation,” and “(it) is a physical sensation.”

Participants will rate the valence of their mental representation on a VAS ranging from negative (0) to positive (100).

3.4.3. Follow-up measures (for previously depressed participants only)

The primary outcome measure of the ‘Disrupting the rhythm of depression’ RCT [31] is the time-related proportion of depressive relapse as assessed using the SCID-I at three, nine, 15 and 24 months (current depressive symptomatology and previous three, six, or nine months). Severity of depressive symptomatology at all time points will be assessed with the HRSD.

3.4.4. Successful tapering of ADM (for previously depressed participants only)

The ADM dose will be assessed during the weekly telephonic interviews. Both a lenient and a stringent operationalization of successful tapering will be used. The lenient operationalization entails an ADM dose reduction of $\geq 50\%$, whereas the stringent operationalization additionally requires that the individual does not relapse into a depressive episode.

The following measures will be included for hypothesis-generating purposes.

3.4.5. Impact of ESM

Additional measures will be included in the questionnaire to explore whether responding to the ‘Imagine your mood’ app may have an impact on affect. After reporting on their emotions and mental representation just before the beep, participants will be asked to assess their current mood on a VAS ranging from happy (0) to sad (100) and their current anxiety (0–100). Furthermore, at the end of the questionnaire participants will be asked to what degree filling out the questionnaire had bothered them (on a 0–100 VAS).

3.4.6. Mental representation

For exploratory reasons, several other aspects of the selected mental representation (what I have in mind ...) will be assessed (on 0–100 VASs). Concrete verbal thinking will be assessed with the questions “I think in words” and “I think in sentences.” Abstract verbal thinking (worry/rumination) has been included in the questionnaire using the following items: “I'm worrying,” “I think about my feelings,” “I wonder why I react the way I do,” and “I analyze the meaning of my feelings.” The intrusiveness will be assessed using the adjectives derived from Brewin et al. [67]: “distressing,” “uncontrollable,” “interfering,” and “vivid.”

Additionally, participants will be asked to rate the degree to which the mental representation is personally relevant (0 = not personally relevant, 100 = personally relevant), whether it refers to “the distant past” (0) or “the far future” (100), and whether they experience the tendency to approach (0) or avoid (100) what they had in mind. Momentary avoidance tendencies will be calculated by averaging this last rating with the rating on the question as to what degree they experience the tendency to approach (0) or avoid (100) their emotions.

3.4.7. Physical complaints

Physical complaints will be assessed with the questions “I feel tired” and the recoded “I feel fit physically” (on 0–100 VASs).

3.4.8. Activities

Participants will be asked to identify their *current activity* and rate this activity on the following scales: “I like doing this,” “this activity requires effort,” “I feel I'm being active” (on 0–100 VASs) and select the category to which the activity belongs.

Participants will be asked to select the most important *previous activity (stressor or event)* in the two hours before the trigger, rate this activity on a VAS that runs from “unpleasant” (0) to “pleasant” (100), and select the category to which the activity belonged.

Finally, participants will be invited to identify the most important *future event* in the next two hours, answer the question “I'm not looking forward to it” (lack of anticipatory pleasure) on a 0–100 VAS and select the category to which the event belongs.

3.5. Analyses

Different analyses will be used for the variety of research questions. The experience sampling data represent repeated measurement within individuals, and this nested structure will be taken into account in all the analyses. An important assumption in many time series analyses is stationarity (i.e. that processes do not change over time). This assumption will be handled either by removing the trends from the data, or by using analyses that do not assume stationarity. Baseline characteristics of never depressed and previously depressed individuals will be compared to examine whether confounding factors may play a role.

First, individual differences in affect will be explored. For examining whether affective changes may signal future relapse, time-varying autoregressive time series models [68] will be fitted for each individual. These models allow for the processes in the data to change over time and are excellently suited for examining the presence of such time-varying processes within individuals. Specifically, the presence of changes in the intercept and autoregressive parameter (see Formula

(1)) are examined to assess the presence of change in mean level and inertia of negative affect. These analyses will be performed both in previously depressed and in never depressed individuals, to examine whether individual affective trajectories are specific to depressive relapse.

$$\text{Negative affect}_{i,t} = \beta_{0,t} + \beta_{1,t} \text{Negative affect}_{i,t-1} + \varepsilon_{i,t}. \quad (1)$$

Second, how imagery-based processing may contribute to affective disturbances in daily life will be explored using mixed linear models. Trends over time will be removed from the data to prevent spurious correlations and data will be person-mean centered. Post-hoc analyses will be used to examine whether findings hold in both the previously depressed and never depressed groups.

Third, it will be examined whether early affective responses can predict successful tapering of ADM by analyzing the data of the first two weeks in the previously depressed participants randomized to PCT while tapering ADM. A bivariate vector-autoregressive Bayesian dynamic model [69] will be performed to model the time structure of the data. More specifically, the mean levels, inertia, and variability will be assessed. Subsequently, it will be examined how these measures of affect and affect dynamics are related to successful tapering of ADM.

Finally, network modeling will be used in two exploratory ways to examine whether relapse prevention strategies in the three treatment arms of the RCT differentially target the network of dynamic interactions between cognitive, behavioral, and affective states. First, group-level network analyses will be used to investigate potential differences in network architecture (e.g. centrality) between the three arms of the trial. Second, as intra-individual network modeling in the context of clinical trial data is still in the developing phase, it will be explored to which extent changes in network architecture over time within individuals can be assessed.

4. Discussion

Both continuation of ADM and psychological interventions can reduce the risk of relapse in previously depressed individuals, but knowledge informing what works best for whom is needed. This micro-trial aims to explore how ESM may inform personalized relapse prevention strategies. Emotions, mental imagery, cognitions, and behaviors will be repeatedly assessed using the smartphone application ‘Imagine your mood’ in a group of previously depressed individuals. The data will be collected alongside a three-armed RCT ‘Disrupting the rhythm of depression’ that investigates what works best in preventing relapse (i.e. continuation of ADM, the combination of ADM with PCT, or tapering ADM combined with PCT). Additionally, a control group of matched never depressed individuals will be included. The relatively limited number of participants included in this micro-trial (45 previously depressed and 15 matched never depressed individuals) will be compensated by the great number of repeated assessments (max 240) within each individual.

In sum, this study will explore four routes to furthering personalized relapse prevention using ESM: individual differences in vulnerability for relapse, processes underlying affective vulnerability, within-individual change while undergoing different relapse prevention strategies and how these relate to successful tapering and prevention of relapse, and differential effects of relapse prevention strategies. These four approaches may be interdependent. For example, examining how cognitive mechanisms contribute to affective vulnerability may be complemented by an understanding of how mechanisms are targeted by different relapse prevention strategies. The data may help unravel the role of individual differences in depressive relapse while undergoing different relapse prevention strategies. This may provide novel information on processes of change as a first step towards improving the protective effect of relapse prevention strategies by tailoring them to individual needs using experience sampling methodology.

Availability of data and materials

Not applicable.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The addition of ESM to the RCT “Disrupting the rhythm of depression” (Netherlands Trial Register: NTR1907) was approved by the medical ethical board of University Medical Center Groningen (METc 2009/158). Ethical approval for including never depressed individuals has been obtained from the University of Groningen Ethical Committee of the Psychology Department (ppo-014-043). The study will be conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent to participate in the study will be obtained from all the participants.

Authors' contributions

CS, CLHB, MHN conceived and designed the study.

CS, CLHB and NB developed the “Imagine your mood” smartphone application and MW gave advice.

CS wrote the first draft of the manuscript.

NSK, CLHB, MHN and MW critically revised the manuscript.

NSK helped setting up the trial.

All authors have read and approved the final manuscript.

Competing interests

CLHB is developer of the preventive cognitive therapy program. All other authors declare that they have no competing interests.

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List of abbreviations

ADM	Antidepressant medication
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
ESM	Experience sampling method
HRSD	Hamilton Rating Scale for Depression
MBCT	Mindfulness based cognitive therapy
MDD	Major depressive disorder
PCT	Preventive cognitive therapy
RCT	Randomized controlled trial
SCID-I	Structured Clinical Interview for axis 1 DSM-IV disorders
VAS	Visual analogue scale

References

- [1] A.J. Ferrari, F.J. Charlson, R.E. Norman, S.B. Patten, G. Freedman, C.J. Murray, T. Vos, H.A. Whiteford, Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010, *PLoS Med.* 10 (11) (2013) 1–12.
- [2] H.A. Whiteford, L. Degenhardt, J. Rehm, A.J. Baxter, A.J. Ferrari, H.E. Erskine, F.J. Charlson, R.E. Norman, A.D. Flaxman, N. Johns, Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010, *The Lancet* 382 (9904) (2013) 1575–1586.
- [3] P.E. Greenberg, A. Fournier, T. Sisitsky, C.T. Pike, R.C. Kessler, The economic burden of adults with major depressive disorder in the United States (2005 and 2010), *J. Clin. Psychiatry* 76 (2) (2015) 155–162.
- [4] D. Richards, Prevalence and clinical course of depression: a review, *Clin. Psychol.*

- Rev. 31 (7) (2011) 1117–1125.
- [5] S.L. Bursuca, W.G. Iacono, Risk for recurrence in depression, *Clin. Psychol. Rev.* 27 (8) (2007) 959–985.
- [6] L.L. Judd, The clinical course of unipolar major depressive disorders, *Arch. Gen. Psychiatry* 54 (11) (1997) 989–991.
- [7] K. Riihimäki, M. Vuorilehto, E. Isometsä, A 5-year prospective study of predictors for functional and work disability among primary care patients with depressive disorders, *Eur. Psychiatry* 30 (1) (2015) 51–57.
- [8] W.W. Eaton, H. Shao, G. Nestadt, B.H. Lee, O.J. Bienvenu, P. Zandi, Population-based study of first onset and chronicity in major depressive disorder, *Arch. Gen. Psychiatry* 65 (5) (2008) 513–520.
- [9] T.E. Moffitt, A. Caspi, A. Taylor, J. Kokaua, B. Milne, G. Polanczyk, R. Poulton, How common are common mental disorders? Evidence that lifetime prevalence rates are doubled by prospective versus retrospective ascertainment, *Psychol. Med.* 40 (6) (2010) 899–909.
- [10] F. Hardeveld, J. Spijker, R. De Graaf, W. Nolen, A. Beekman, Prevalence and predictors of recurrence of major depressive disorder in the adult population, *Acta Psychiatr. Scand.* 122 (3) (2010) 184–191.
- [11] P. Glue, M.R. Donovan, S. Kolluri, B. Emir, Meta-analysis of relapse prevention antidepressant trials in depressive disorders, *Aust. N. Z. J. Psychiatry* 44 (8) (2010) 697–705.
- [12] R. Hansen, B. Gaynes, P. Thieda, G. Gartlehner, A. veaugh-Geiss, E. Krebs, K. Lohr, Prevention of major depressive disorder relapse and recurrence with second-generation antidepressants: a systematic review and meta-analysis, *Psychiatr. Serv.* 59 (10) (2008) 1121–1130.
- [13] J. Guidi, G. Fava, M. Fava, G. Papakostas, Efficacy of the sequential integration of psychotherapy and pharmacotherapy in major depressive disorder: a preliminary meta-analysis, *Psychol. Med.* 41 (2) (2011) 321–331.
- [14] J.R. Vittengl, L.A. Clark, T.W. Dunn, R.B. Jarrett, Reducing relapse and recurrence in unipolar depression: a comparative meta-analysis of cognitive-behavioral therapy's effects, *J. Consult Clin. Psychol.* 75 (3) (2007) 475–488.
- [15] J. Piet, E. Hougaard, The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: a systematic review and meta-analysis, *Clin. Psychol. Rev.* 31 (6) (2011) 1032–1040.
- [16] K. Clarke, E. Mayo-Wilson, J. Kenny, S. Pilling, Can non-pharmacological interventions prevent relapse in adults who have recovered from depression? A systematic review and meta-analysis of randomised controlled trials, *Clin. Psychol. Rev.* 39 (2015) 58–70.
- [17] K.E. Biesheuvel-Leliefeld, G.D. Kok, C.L.H. Bockting, P. Cuijpers, S.D. Hollon, H.W. van Marwijk, F. Smit, Effectiveness of psychological interventions in preventing recurrence of depressive disorder: meta-analysis and meta-regression, *J. Affect Disord.* 174 (2015) 400–410.
- [18] A.E. Kazdin, Evidence-based psychosocial treatment: advances, surprises, and needed shifts in foci, *Cogn. Behav. Pract.* 23 (4) (2016) 426–430.
- [19] R. Uher, The implications of gene–environment interactions in depression: will cause inform cure? *Mol. Psychiatry* 13 (12) (2008) 1070–1078.
- [20] G.E. Simon, R.H. Perlis, Personalized medicine for depression: can we match patients with treatments? *Am. J. Psychiatry* 167 (12) (2010) 1445–1455.
- [21] C.L.H. Bockting, S.D. Hollon, R.B. Jarrett, W. Kuyken, K. Dobson, A lifetime approach to major depressive disorder: the contributions of psychological interventions in preventing relapse and recurrence, *Clin. Psychol. Rev.* 41 (2015) 16–26.
- [22] W. Kuyken, F.C. Warren, R.S. Taylor, B. Whalley, C. Crane, G. Bondolfi, R. Hayes, M. Huijbers, H. Ma, S. Schweizer, Efficacy of mindfulness-based cognitive therapy in prevention of depressive relapse: an individual patient data meta-analysis from randomized trials, *JAMA psychiatry* 73 (6) (2016) 565–574.
- [23] S. Shiffman, A.A. Stone, M.R. Hufford, Ecological momentary assessment, *Annu. Rev. Clin. Psychol.* 4 (2008) 1–32.
- [24] I. Myin-Germeyns, M. Oorschot, D. Collip, J. Lataster, P. Delespaul, J. van Os, Experience sampling research in psychopathology: opening the black box of daily life, *Psychol. Med.* 39 (09) (2009) 1533–1547.
- [25] M. Csikszentmihalyi, R. Larson, Validity and reliability of the experience-sampling method, *J. Nerv. Ment. Dis.* 175 (9) (1987) 526–536.
- [26] J. van Os, S. Verhagen, A. Marsman, F. Peeters, M. Bak, M. Marcelis, M. Drukker, U. Reininghaus, N. Jacobs, T. Lataster, C. Simons, I.P. ESM-MERGE, R. Lousberg, S. GÅ¼AIAkÅ¼, C. Leue, P.C. Groot, W. Viechtbauer, P. Delespaul, The experience sampling method as an mHealth tool to support self-monitoring, self-insight, and personalized health care in clinical practice, *Depress Anxiety* 34 (6) (2017) 1–13.
- [27] C. Simons, J. Hartmann, I. Kramer, C. Menne-Lothmann, P. Höhn, A. Van Bommel, I. Myin-Germeyns, P. Delespaul, J. Van Os, M. Wichers, Effects of momentary self-monitoring on empowerment in a randomized controlled trial in patients with depression, *Eur. Psychiatry* 30 (8) (2015) 900–906.
- [28] I. Kramer, C.J. Simons, J.A. Hartmann, C. Menne-Lothmann, W. Viechtbauer, F. Peeters, K. Schruers, A.L. Bommel, I. Myin-Germeyns, P. Delespaul, A therapeutic application of the experience sampling method in the treatment of depression: a randomized controlled trial, *World Psychiatry* 13 (1) (2014) 68–77.
- [29] W.N. Morris, The mood system, in: D. Kahneman, E. Diener, N. Schwarz (Eds.), *Wellbeing: the Foundations of Hedonic Psychology*, Russell Sage Foundation, New York, NY, 1999, pp. 169–189.
- [30] S. Verhagen, L. Hasmi, M. Drukker, J. van Os, P. Delespaul, Use of the experience sampling method in the context of clinical trials, *Evid. Based Ment. Health* 19 (3) (2016) 86–89.
- [31] C.L.H. Bockting, H.J. Elgersma, G.D. van Rijsbergen, P. de Jonge, J. Ormel, E. Buskens, A.D. Stant, P. de Jong, F. Peeters, M. Huijbers, A. Arntz, P. Muris, W. Nolen, A. Schene, S. Hollon, Disrupting the rhythm of depression: design and protocol of a randomized controlled trial on preventing relapse using brief cognitive
- therapy with or without antidepressants, *BMC Psychiatry* 11 (12) (2011) 1–9.
- [32] American Psychiatric Association, Practice Guideline for the Treatment of Patients with Major Depressive Disorder, third ed., (2010).
- [33] K. Kelly, M. Posternak, J.E. Alpert, Toward achieving optimal response: understanding and managing antidepressant side effects, *Dialogues Clin. Neurosci.* 10 (4) (2008) 409–418.
- [34] C. Cartwright, K. Gibson, J. Read, O. Cowan, T. Dehar, Long-term antidepressant use: patient perspectives of benefits and adverse effects, *Patient Prefer. Adherence* 10 (2016) 1401–1407.
- [35] M.C. ten Doesschate, C.L.H. Bockting, A.H. Schene, Adherence to continuation and maintenance antidepressant use in recurrent depression, *J. Affect Disord.* 115 (1–2) (2009) 167–170.
- [36] C.L.H. Bockting, M.C. ten Doesschate, J. Spijker, P. Spinhoven, M.W. Koeter, A.H. Schene, DELTA study group: continuation and maintenance use of antidepressants in recurrent depression, *Psychother. Psychosom.* 77 (1) (2008) 17–21.
- [37] G.A. Fava, A. Gatti, C. Belaise, J. Guidi, E. Offidani, Withdrawal symptoms after selective serotonin reuptake inhibitor discontinuation: a systematic review, *Psychother. Psychosom.* 84 (2) (2015) 72–81.
- [38] K.S. Dobson, S.D. Hollon, S. Dimidjian, K.B. Schmaling, R.J. Kohlenberg, R.J. Gallop, S.L. Rizvi, J.K. Gollan, D.L. Dunner, N.S. Jacobson, Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the prevention of relapse and recurrence in major depression, *J. Consult Clin. Psychol.* 76 (3) (2008) 468–477.
- [39] S.D. Hollon, M.O. Stewart, D. Strunk, Enduring effects for cognitive behavior therapy in the treatment of depression and anxiety, *Annu. Rev. Psychol.* 57 (2006) 285–315.
- [40] M.A. Prins, P.F. Verhaak, J.M. Bensing, K. van der Meer, Health beliefs and perceived need for mental health care of anxiety and depression—the patients' perspective explored, *Clin. Psychol. Rev.* 28 (6) (2008) 1038–1058.
- [41] D.J. van Schaik, A.F. Klijn, H.P. van Hout, H.W. van Marwijk, A.T. Beekman, M. de Haan, R. van Dyck, Patients' preferences in the treatment of depressive disorder in primary care, *Gen. Hosp. Psychiatry* 26 (3) (2004) 184–189.
- [42] C.L.H. Bockting, A.H. Schene, P. Spinhoven, M.W.J. Koeter, L.F. Wouters, J. Huyser, J.H. Kamphuis, Preventing relapse/recurrence in recurrent depression with cognitive therapy: a randomized controlled trial, *J. Consult Clin. Psychol.* 73 (4) (2005) 647–657.
- [43] J.D. Teasdale, Z.V. Segal, J.M.G. Williams, V.A. Ridgeway, J.M. Soulsby, M.A. Lau, Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy, *J. Consult Clin. Psychol.* 68 (4) (2000) 615–623.
- [44] G.A. Fava, C. Rafanelli, S. Grandi, S. Conti, P. Belluardo, Prevention of recurrent depression with cognitive behavioral therapy: preliminary findings, *Arch. Gen. Psychiatry* 55 (9) (1998) 816–820.
- [45] W. Kuyken, R. Hayes, B. Barrett, R. Byng, T. Dalgleish, D. Kessler, G. Lewis, E.R. Watkins, C. Brejcha, J. Cardy, Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial, *The Lancet* 386 (9988) (2015) 63–73.
- [46] M.J. Huijbers, P. Spinhoven, J. Spijker, H.G. Ruhe, D.J. van Schaik, P. van Oppen, W.A. Nolen, J. Ormel, W. Kuyken, G.J. van der Wilt, M.B. Blom, A.H. Schene, A.R. Donders, A.E. Speckens, Discontinuation of antidepressant medication after mindfulness-based cognitive therapy for recurrent depression: randomised controlled non-inferiority trial, *Br. J. Psychiatry* 208 (4) (2016) 366–374.
- [47] B. Hosenfeld, E.H. Bos, K.J. Wardenaar, H.J. Conradi, Maas van der, L.J. Han, I. Visser, P. de Jonge, Major depressive disorder as a nonlinear dynamic system: bimodality in the frequency distribution of depressive symptoms over time, *BMC Psychiatry* 15 (2015) 1–9.
- [48] E.I. Fried, R.M. Nesse, Depression is not a consistent syndrome: an investigation of unique symptom patterns in the STAR* D study, *J. Affect Disord.* 172 (2015) 96–102.
- [49] I.A. van de Leemput, M. Wichers, A.O. Cramer, D. Borsboom, F. Tuerlinckx, P. Kuppens, E.H. van Nes, W. Viechtbauer, E.J. Giltay, S.H. Aggen, C. Derom, N. Jacobs, K.S. Kendler, H.L. van der Maas, M.C. Neale, F. Peeters, E. Thiery, P. Zachar, M. Scheffer, Critical slowing down as early warning for the onset and termination of depression, *Proc. Natl. Acad. Sci. U*

- [58] G.D. van Rijsbergen, S.D. Hollon, H.J. Elgersma, G.D. Kok, J. Dekker, A.H. Schene, C.L. Bockting, Understanding emotion and emotional scarring in recurrent depression, *Compr. Psychiatry* 59 (2015) 54–61.
- [59] G.D. van Rijsbergen, C.L.H. Bockting, M. Berking, M.W. Koeter, A.H. Schene, Can a one-item mood scale do the trick? Predicting relapse over 5.5-years in recurrent depression, *PloS One* 7 (10) (2012) e46796.
- [60] J.M. Bakker, R. Lieverse, N. Geschwind, F. Peeters, I. Myin-Germeys, M. Wichers, The two-sided face of antidepressants: the impact of their use on real-life affective change during mindfulness-based cognitive therapy, *Psychother. Psychosom.* 85 (3) (2016) 180–182.
- [61] M.B. First, R.L. Spitzer, M. Gibbon, J.B. Williams, User's Guide for the Structured Clinical Interview for DSM-IV axis I Disorders SCID-I: Clinician Version, American Psychiatric Pub, 1997.
- [62] M. Hamilton, A rating scale for depression, *J. Neurol. Neurosurg. Psychiatry* 23 (1960) 56–62.
- [63] C.L.H. Bockting, Preventie Cognitieve Training bij Terugkerende Depressie Houten, Bohn Stafleu van Loghum, 2009.
- [64] National Collaborating Centre for Mental Health, Depression: Management of Depression in Primary and Secondary Care, London: National Institute for Clinical Excellence, 2004, p. 24.
- [65] Anonymous Proceedings of the Proceedings of the 7th Nordic Conference on Human-computer Interaction: Making Sense through Design, ACM, 2012.
- [66] M. Wichers, Z. Kasanova, J. Bakker, E. Thiery, C. Derom, N. Jacobs, J. van Os, From affective experience to motivated action: tracking reward-seeking and punishment-avoidant behaviour in real-life, *PloS One* 10 (6) (2015) 1–16.
- [67] C.R. Brewin, J. Wheatley, T. Patel, P. Fearon, A. Hackmann, A. Wells, P. Fisher, S. Myers, Imagery rescripting as a brief stand-alone treatment for depressed patients with intrusive memories, *Behav. Res. Ther.* 47 (7) (2009) 569–576.
- [68] L.F. Bringmann, E.L. Hamaker, D.E. Vigo, A. Aubert, D. Borsboom, F. Tuerlinckx, Changing dynamics: time-varying autoregressive models using generalized additive modeling, *Psychol. methods* (2016) 1–17.
- [69] T. Krone, C.J. Albers, M.E. Timmerman, Bayesian dynamic modelling to assess differential treatment effects on panic attack frequencies, *Stat. Model.* 16 (2016) 343–359.